REMARKS

Claims 1-30, 113-119, and 136-152 are currently pending. New claims 153-154 have been added. Support for new claims 153-154 can be found in the specification at page 35, lines 7-8. Claims 144 and 145 have been withdrawn as directed to a non-elected invention. Claims 2-3, 117, 147, and 151-152 are cancelled without prejudice to their patentability. Claims 1, 4, 9, 10, 29, 113, 136-140, 146, and 148 are amended without prejudice to their patentability.

Although claims 113, 136, 146, and 148 have been amended to depend from claim 1, applicants respectfully reserve the right to submit claims during further prosecution of this application or in a continuation or divisional thereof, directed to the previous version of these claims.

Phone Interview

The courteous telephone interview granted by Examiners Ford and Minnifield to Applicants' representatives John Roedel and Laura Hilmert is respectfully acknowledged.

During the phone interview, Applicants' attorneys proposed an amendment to claim 1 requiring that oocysts be separated from bacterial contaminants by tangential flow filtration. The Examiners questioned whether the form of the amendment as then proposed was effective to impose any structural limitation on the claimed composition, or instead was merely a bare process limitation. Discussion during the interview dealt primarily with this issue. Applicants' representatives did not understand the Examiners to contest the novelty of a claim amended to impose a limitation on bacterial contaminants.

In light of the interview, the form of claim as now presented includes additional language specifying a limitation on bacterial contaminants that was not expressly stated in the form of claim discussed during the interview.

Amendments

It is respectfully submitted that a structural limitation on bacterial contaminants is expressly imposed by claim 1 as currently amended. More particularly, claim 1 requires the presence of oocysts that have been obtained from a source which contains bacterial contaminants, as is normally if not universally the case. The claim further characterizes the composition as:

> "being substantially free of bacterial contaminants which are present in said source but have been separated from said oocysts by tangential flow filtration of an aqueous process medium containing said oocysts and said bacterial contaminants..."

The claim more specifically requires that separation of the bacterial contaminants is accomplished:

> "using a filter membrane having a pore size such that sporulated oocysts cannot enter the pores, but said bacterial contaminants can pass through the pores."

The substantial exclusion of such bacterial contaminants from the composition is a structural limitation which is respectfully submitted as distinguishing the claimed composition from the references of record.

It is further respectfully submitted that amended claim 1 is in proper form as a product-by-process claim. As stated in the MPEP:

> The structure implied by the process steps should be considered when assessing the patentability of product-by-process claims over the prior art, especially where the product can only be defined by the process steps by which the product is made, or where the manufacturing process steps would be expected to impart distinctive structural characteristics to the final product.[1]

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[1]MPEP §2113 (emphasis added).

Both the express substantial exclusion of "bacterial contaminants which are present in said source" and the product-by-process limitations impose a structural limitation on the claim. More particularly, Applicants submit that a "distinctive structural characteristic" is imparted by the specified requirement of tangential flow filtration using:

> "a filter membrane having a pore size such that sporulated oocysts cannot enter the pores, but said bacterial contaminants can pass through the pores"

Moreover, the instant invention further qualifies for product-by-process protection because the residual content of bacterial contaminants has not been quantified.

Support for the phrase "derived from an oocysts source comprising bacterial contamination" in amended claim 1 can be found in the specification at page 13, lines 6-10, which states that oocysts can be collected from feces, intestinal contents and/or scrapings, and contaminated bedding. As recognized by those skilled in the art, such oocysts sources inherently comprise bacterial contamination.

Support for separating bacterial contaminants from the oocysts by tangential flow filtration of an aqueous process medium containing the oocysts and the bacterial contaminants can be found in the specification at pages 34-35, which state that tangential flow filtration is used to separate sporulated oocysts from the sporulation medium[2] and from other materials, such as other microorganisms, that may be present in the oocyst suspension.[3] Support may also be found on pages 38-39, which describe performing tangential flow filtration after sterilization of the sporulated oocysts. Specific

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[2] The sporulation medium comprises the oocysts, and inherently comprises the bacterial contaminants, since the oocysts in the sporulation medium are those originally derived from feces, intestinal contents and/or scrapings, and contaminated bedding, as previously discussed.

[3] *See, e.g.*, Specification, p. 34, ln. 29 to p. 35, ln. 1 ("Tangential flow filtration ("TFF") is used in this procedure to separate sporulated oocysts from other material that may be present in the suspension, e.g., grit, other microorganisms, etc.").

support for using a filter membrane having a pore size small enough so that sporulated oocysts cannot enter the pores, but bacterial contaminants can pass through the pores can be found on page 35, lines 5-8.

Independent claims 9 and 10 have been amended in a manner similar to claim 1. In addition, former independent claims 113, 136, 146, and 148 have now been amended, without prejudice to their patentability, to depend from claim 1.

Rejections under 35 U.S.C. §102(a)

Reconsideration is respectfully requested of the rejection of claims 1, 4-22, 29-30, 113-116, 118-119, 136-141, 146, and 148-150 under 35 U.S.C. §102(b) as anticipated by Conkle, et al. (WO 00/50072).

As amended, claim 1 is directed to a composition for the prevention or control of coccidiosis. The composition comprises viable sporulated oocysts that are derived from an oocysts source comprising bacterial contamination and that comprise at least one species of protozoa known to cause coccidiosis. The composition is sterile, contains at least about 10,000 oocysts per milliliter and less than about 0.4% by weight of alkali metal dichromate. The composition is substantially free of bacterial contaminants which are present in the source but have been separated from the oocysts by tangential flow filtration of an aqueous process medium containing the oocysts and the bacterial contaminants using a filter membrane having a pore size such that sporulated oocysts cannot enter the pores, but the bacterial contaminants can pass through the pores.

As defined in amended claim 1, distinct advantages are possessed by applicant's novel composition for prevention or control of coccidiosis. The composition is not only substantially or entirely free of potassium dichromate, but is also substantially free of bacterial contaminants derived from the oocyst source.

By substantially excluding bacterial contaminants derived from the source of oocysts, it is respectfully submitted that claim 1 distinguishes the teachings of Conkle, et al. under 35 U.S.C. §102. It is recognized that Conkle, et al. teach the treatment of their

compositions with antibacterial agents such as hydrogen peroxide or sodium hypochlorite. However, it is important to understand that "bacterial contaminants," as specified in claim 1 encompass not only live bacteria, but non-viable contaminants such as dead bacteria and cellular debris that remain after treatment with a anti-bacterial agent. Treatment according to Conkle, et al. may be effective for killing bacteria, but Conkle, et al. fail to teach or suggest removal of non-viable bacteria or bacterial debris, whether by tangential flow filtration or otherwise.

As specified in claim 1, since the pore size of the filter membrane used during tangential flow filtration is large enough to allow bacteria to pass through, the oocysts retained by the filter membrane have been separated from both viable and non-viable contaminants, such as bacteria and cellular debris. The oocysts in the composition of amended claim 1 thus contain a much lower amount of bacterial contaminants (both viable and non-viable) than would be present were the pore size small enough to retain bacteria as well as oocysts.

As is known to those skilled in the art, the presence of contaminants, such as non-viable bacterial contaminants, in a vaccine composition increases the risk of producing a pyrogenic reaction in vaccinated animals.[4] Consequently, the composition of claim 1 provides an advantage over other compositions, such as the compositions of Conkle, et al., in that the lower amount of non-viable bacterial contaminants reduces the risk that animals administered the composition will experience a pyrogenic reaction.

Conkle et al. particularly fail to disclose or suggest an oocyst-containing composition that is substantially free of bacterial contaminants that are present in a source but that have been separated from the oocysts by tangential flow filtration of a aqueous process medium containing the oocysts and the bacterial contaminants using a

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[4] Methods for determining whether a pyrogenic reaction occurs are well known in the art.

filter membrane with a pore size small enough to prevent sporulated oocysts from entering the pores, but large enough to allow bacteria to pass through the pores.

For example, Conkle, et al. state that oocysts may be washed following sporulation to reduce the residual oxidant concentration to an acceptable level. Serial washings may be conducted, preferably by membrane filtration, and more preferably by diafiltration. Serial washing or diafiltration may also be used after bleaching to reduce the residual oxidant concentration in the bleached suspension (e.g., the concentration of sodium hypochlorite in the suspension), to an acceptable level.[5] Significantly, however, Conkle, et al. do not disclose the use of a filter pore size small enough to prevent sporulated oocysts from entering the pores, but large enough to allow bacteria to pass through the pores. Rather, the only mention in Conkle, et al. of pore size is a statement that in the case of membrane filtration, "the membrane pore size is selected to allow passage of solutes through the membrane while restricting the passage of the oocysts from one side of the membrane to the other."[6] There is no statement or suggestion in Conkle, et al. that the pore size should also be large enough to allow the passage of bacteria, as well as solutes. In fact, such a pore size would not be necessary to achieve the stated purpose of washing in Conkle, et al., i.e., to reduce the residual oxidant concentration to an acceptable level. There is no suggestion of the desirability of separating the oocysts from bacterial or other contaminants that may be present in the sporulation medium, or in the bleached oocyst suspension. Consequently, in contrast to the composition of amended claim 1, the oocyst-containing compositions of Conkle, et al. are not, either expressly or inherently, substantially free of bacterial contaminants which are present in a source but have been separated from the oocysts by tangential flow filtration of an aqueous process medium containing the oocysts and the bacterial

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[5] "Following bleaching, the bleached suspension is washed, if necessary, to reduce the residual oxidant concentration to an acceptable level." Conkle, et al., p. 8, ln. 33-35.

[6] Conkle, et al., p. 8, ln. 19-20 (emphasis added).

contaminants (including non-viable bacterial contaminants) using a filter membrane having a pore size such that sporulated oocysts can not enter the pores, but bacteria can pass through the pores.

The composition of Conkle, et al. thus can be said to comprise a greater amount of non-viable bacterial contaminants than the composition of amended claim 1. In fact, Conkle, et al. openly recognize that some solids of bacterial dimension or larger may remain in the final suspension. For example, Conkle, et al. state: "the final concentrated encysted protozoa suspension can include a maximum solids size of less than about 200 microns, preferably less than about 25 microns, a salt content of less than about 0.96 percent...and a cyst concentration of about 1 x 10^6 to 2.5 x 10^6 cysts/ml."[7]

Thus, Conkle, et al. manifestly fail to describe each and every element of claim 1.[8] Applicants thus submit that claim 1 is patentable under 35 U.S.C. §102(b) over Conkle, et al.

Claims 4-8, 14-22, 29-30, and new claims 153-154 depend either directly or indirectly from claim 1 and are thus patentable for the same reasons as set forth above for claim 1 as well as for the additional elements they require.

Like claim 1, claims 9 and 10 are directed to compositions comprising sporulated oocysts, and have been amended in a manner similar to that of claim 1. Claims 9 and 10, as well as claims 11-13 which depend either directly or indirectly from claim 10, are thus patentable for the same reasons as set forth above for claim 1, as well as for the additional elements they require.

Claim 136 has been amended, without prejudice to its patentability, to depend from claim 1. Claim 136, as well as claims 137-141 which depend directly or indirectly

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[7] *Id.* at p. 8, ln. 38 to p. 9, ln. 3.

[8] MPEP §2131 states that a claim is anticipated under 35 U.S.C. §102 only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference.

from claim 136, are thus patentable for the same reasons as set forth above for claim 1, as well as for the additional elements they require.

Claim 146 has been amended, without prejudice to its patentability, to depend from claim 1. Claim 146, as well as claims 149-150 which depend either directly or indirectly from claim 146, are thus patentable for the same reasons as set forth above for claim 1 as well as for the additional elements they require.

Claim 148 has been amended, without prejudice to its patentability, to depend from claim 1 and is thus patentable for the same reasons as set forth above for claim 1 as well as for the additional elements it requires.

Claim 113

Amended claim 113, directed to a kit comprising the composition of claim 1 and instructions for administration fo the composition to an animal, has been amended, without prejudice to its patentability, to depend from claim 1. Claim 113 is thus patentable for the same reasons as set forth above for claim 1 as well as for the additional elements it requires.

The Office has also reiterated its previous rejection of claim 113, stating that a package insert, such as instructions, does not lend patentable weight to the claim, absent a functional relationship between the instructions and the composition. The Office has further stated that the instructions are a limitation of intended use and if the composition of Conkle, et al. is capable of performing the intended use, then it meets the claim.

Applicants again respectfully submit that the instructions in the kit of claim 113 constitute more than a mere intended use; they are functionally related to the composition, and therefore should be given patentable weight.[9] Claim 113 is directed to

[9] "Under section 103, the board cannot dissect a claim, excise the printed matter from it, and declare the remaining portion of the mutilated claim to be unpatentable. The claim must be read as a whole." *In re Gulack*, 217 USPQ 401, 403 (Fed. Cir. 1983). Furthermore,

a kit for the prevention or control of coccidiosis, comprising the composition and the instructions for administration of the composition to an animal; claim 113 is not directed to either the composition or instructions alone. Furthermore, the compositions of the present invention may be administered by a variety of routes, and may require dilution before administration.[10] The instructions in claim 113 are for administration of the composition to an animal, and are thus functionally related to the composition since they allow the user of the kit to gain the additional benefit of a properly prepared and administered composition. Claim 113 is thus patentable under 35 U.S.C. §102(b) over Conkle, et al. for this additional reason.

Claims 114-116 and 118-119 depend directly or indirectly from claim 113 and are thus patentable for the same reasons as set forth above for claim 113 as well as for the additional elements they require.

Claim 139

As discussed above, claim 139 depends indirectly on claim 136 and is thus patentable for the same reasons as set forth above for claim 136. In addition, applicants respectfully submit that the phrase "...a ratio defined by the minimum immunizing dose and amount determined by storage half-life determinations" is more than a mere limitation of intended use, and that it cannot be found inherently in Conkle, et al. based on the reference's general disclosure that encysted protozoa oocysts including *Eimeria*

"[t]he fact that printed matter by itself is not patentable subject matter, because non-statutory, is no reason for ignoring it when the claim is directed to a combination." *In re Miller*, 164 USPQ 46, 49 (C.C.P.A. 1969).

[10] "The vaccine may be concentrated, requiring dilution before administration, or the vaccine may be ready for administration. The concentrated embodiment of the instant invention may be diluted with any suitable diluent to concentrations suitable for various forms of administration, including intra-yolk sac administration, per os, oral gavage, delivery via spray cabinet, or top-fed via spray onto food, such as OASIS Hatchling Supplement." Specification, p. 46, ln. 15-20.

maxima, E. mitis, E. tenella, E. acervulina, E. brunetti, E. necatrix, E. praecox, and mixtures thereof can be given in a single vaccine.

The phrase "in a ratio defined by the minimum immunizing dose and amount determined by storage half-life determinations" does not specify any intended use of the composition as a whole, but instead quantifies the amounts of *E. acervulina, E. maxima,* and *E. tenella* sporulated oocysts and ratios thereof that are present in the composition.[11] Since a certain number of sporulated oocysts cease to be functional as they age, the minimum number of sporulated oocysts of each *Eimeria* species in the composition may be determined using the minimum immunizing dose and the storage half-life of the sporulated oocysts. As those skilled in the art will readily understand from Applicants' specification, the half life defines the slope of the logarithmic decay curve. Back projection on this curve over a period corresponding to storage life defines the amount of oocysts that must be contained in the original dose package in order to assure that minimum immunizing dose remains on the day of administration.[12]

The Office has provided no evidence to support its stated conclusion that the claim limitation "a ratio is defined by the minimum immunizing dose and amount determined by storage half-life determinations" is inherent in Conkle, et al. To establish inherency, "the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic

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[11] "The combined species of sporulated oocysts are present in a number sufficient to comprise the minimum number of sporulated oocysts required to comprise an effective dose for immunizing purposes." Specification, p. 45, ln. 18-21.

[12] "The number of sporulated oocysts per dose is further determined by the estimated half-life of the sporulated oocysts in the storage composition claimed herein. As the sporulated oocysts age a certain number cease to be functional...Therefore, a minimum amount of a single species or combination of sporulated oocysts is added to the compositions for consumption that will result in the minimum immunizing dose computed as a function of half-life determinations." *Id.* at ln. 21-27.

necessarily flows from the teachings of the applied prior art."[13] "The fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic."[14] Conkle, et al. do not describe any ratio of *E. acervulina*, *E. maxima*, and *E. tenella* sporulated oocysts present in their composition. As previously discussed, Conkle, et al. merely state that the coccidial oocysts can be *E. maxima*, *E. mitis*, *E. tenella*, *E. acervulina*, *E. brunetti*, *E. necatrix*, *E. praecox*, and mixtures thereof, but do not disclose or suggest any ratio of oocysts. Furthermore, Conkle, et al. do not discuss the aging of sporulated oocysts or determining a suitable amount of oocysts by storage half-life determinations. Consequently, the compositions of Conkle, et al. cannot be said to *necessarily* comprise sporulated oocysts of *E. acervulina*, *E. maxima*, and *E. tenella* in a ratio defined by the minimum immunizing dose and amount determined by storage half-life determinations, as required by claim 139. Conkle, et al. can thus not be said to describe all the limitations of claim 139, and claim 139 is thus also patentable for this further reason.

Moreover, the Examiner's contention that pharmaceutical compositions administered in immunizing doses "can include determination by storage half life determinations" is undocumented by any source other than applicant's specification. And even if the proposition stated by the Examiner were accepted as known art, it does not meet the requirement of claim 139 that "sporulated oocysts of *Eimeria acervulina*, *Eimeria maxima*, and *Eimeria tenella*" are present "in a ratio defined by the minimum immunizing dose and amount determined by storage half-life determinations."

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[13] MPEP § 2112 (citing *Ex parte Levy*, 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990) (emphasis in original)).

[14] MPEP §2112 (citing *In re Rijckaert*, 9 F.3d 1531, 1534 (Fed. Cir. 1993)). MPEP §2112 also states "[i]nherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient." (quoting *In re Robertson*, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999).

In light of the foregoing, applicants respectfully request withdrawal of the rejection of claims 1, 4-22, 29-30, 113-116, 118-119, 136-142, 146, and 148-150 under 35 U.S.C. §102(b), and allowance of these and new claims 153-154.

Rejections under 35 U.S.C. §103(a)

Reconsideration is requested of the rejection of claims 1, 4-30, 113-116, 118-119, 136-143, 146, and 148-150 under 35 U.S.C. §103(a) as unpatentable over Conkle, et al. (WO 00/50072), in view of Brown, et al. (U.S. Patent No. 6,019,985).

Other than the disclosure of *P. acnes*, Applicants are unable to identify anything which Brown, et al. add to the teachings of Conkle, et al. Nor has the Examiner identified any other teaching of Brown, et al. that is relevant the compositions as claimed herein. Thus, citation of the Brown, et al. reference would appear to have relevance only with respect to claims 23-28, 142, and 143, which call for a component composition which ameliorates a decline in post-challenge performance, and specifically to claims 26-28 and 143 which expressly call for the presence of *P. acnes*.

Consequently, Applicants are at a loss to understand the §103 rejection of claims 1, 4-22, 29, 30, 113-116, 118, 119, 136-141, 146 or 148-150. Since none of these claims have been rejected under §103 on the basis of Conkle, et al. alone, there would not seem to be any basis on which they could be found obvious from Conkle, et al. in view of Brown, et al.

In any event, Applicants respectfully submit that all claims define patentably over Conkle et al., and over any combination of Conkle, et al. and Brown, et al. under §103. Since there is no disclosure or suggestion in either Conkle, et al. or in Brown, et al. (nor any motivation to modify the cited references) of oocyst containing compositions that are substantially free of bacterial contaminants which are present in a source but have been separated from the oocysts by tangential flow filtration of an aqueous process medium containing the oocysts and the bacterial contaminants using a filter membrane having a pore size such that sporulated oocysts cannot enter the pores, but the bacterial

contaminants can pass through the pores, it is respectfully submitted that claim 1 is patentable over Conkle, et al., and over any combination of Conkle, et al. with Brown, et al.

Since, as previously discussed, claims 4-30, 113-116, 118-119, 136-143, 146, 148-150, and new claims 153-154 now depend either directly or indirectly from claim 1, they are also patentable over Conkle, et al., and over any combination of Conkle, et al. with Brown, et al., for the same reasons as set forth above for claim 1.

Rejection Under 35 U.S.C. §112, first paragraph

Reconsideration is requested of the rejection of claims 1, 4-30, 113-116, 118-119, 136-143, 146, and 148-150 under 35 U.S.C. §112, first paragraph. Specifically, the Office has stated that the term "non-attenuated" is new matter and is not supported by the original disclosure.

Claims 1, 9, 10, 113, 136-140, and 148 have been amended to remove the term "non-attenuated." Applicants thus submit that claims 1, 9, 10, 113, 136-140, and 148 are patentable under 35 U.S.C. §112, first paragraph.

Claims 4-8, 11-30, 114-116, 118-119, 141-143, 146, and 149-150 depend either directly or indirectly from claim 1 and are thus patentable for the same reasons for claim 1.

Applicants respectfully reserve the right to submit claims during further prosecution of this application, or in a continuation or divisional thereof, in which the oocysts are characterized as "non-attenuated." Although the issue has been mooted in the instant application by the amendments made herein, Applicants' remain of the view that the term "non-attenuated" has §112 support.

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CONCLUSION

In light of the foregoing, applicants respectfully request withdrawal of the rejection of claims 1, 4-30, 113-116, 118-119, 136-143, 146, and 148-150, and allowance of these and new claims 153-154.

The Commissioner is hereby authorized to charge $120.00 for a one month extension of time, as well as any other fees due in connection with this response, to Deposit Account No. 19-1345.

Respectfully submitted,

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